AMENDMENTS

Please amend the subject application as set forth below.

In the Claims

Cancel claims 40 through 81 inclusive without prejudice.

Add new claims 82 through 101 inclusive as set forth below.

Pursuant to 37 CFR 1.121, a complete listing of all the claims as amended of the subject application, which is a continued prosecution application (CPA) filed on 26 September 2002, is set out below; treating, for purposes of 37 CFR 1.121(c), the continued prosecution application (CPA) filed on 26 September 2002 and its immediate parent application which was filed on 26 February 1999 as a single application.

Claims 1 through 81 inclusive (cancelled).

82. (New) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target

nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, at least one deoxynucleotide defining a labeled deoxynucleotide comprising a detectable label or an attachment moiety capable of binding a detectable label, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled deoxynucleotide is complementary to a specific nucleotide at the predetermined target position, a detectable primer-extension product is formed of the detection primer extended to include an extension portion incorporating the labeled deoxynucleotide; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of a detectable label in association with a labeled deoxynucleotide incorporated in an extension portion of a primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

83. (New) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a

deoxynucleotide is complementary to a specific nucleotide at the predetermined target position, a detectable nucleotide-identifier primer-extension product is formed of the detection primer extended to include an extension portion incorporating the deoxynucleotide, the detectable nucleotide-identifier primer-extension product being detectably different from the detection primer and from any alternative primer-extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of the detectable nucleotide-identifier primer-extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

84. (New) A method according to claim 83

wherein at least one deoxynucleotide of the admixture of nucleoside triphosphates of step (c) defines a labeled deoxynucleotide comprising a detectable label or an attachment moiety capable of binding a detectable label, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled deoxynucleotide is complementary to a specific nucleotide at the predetermined target position, the detectable nucleotide-identifier primer-extension product is formed of the detection primer extended to include an extension portion incorporating the labeled deoxynucleotide, the incorporation of the labeled deoxynucleotide in the extension portion of the detectable nucleotide-identifier primer-extension product rendering the primer-extension product detectably different from the detection primer and from any alternative primer-extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position, and

wherein the step (d) of analyzing the extension-reaction mixture from step (c) for the presence or absence of the detectable nucleotide-identifier primer-extension product includes analyzing the extension-reaction mixture for the presence or absence of a detectable label in association with a labeled deoxynucleotide incorporated in an extension portion of a primer

extension product to determine the respective presence or absence of the detectable nucleotide-identifier primer-extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

85. (New) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, at least one chain-

terminating nucleotide analogue defining a labeled chain-terminating nucleotide analogue comprising a detectable label or an attachment moiety capable of binding a detectable label, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled chain-terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined target position, a detectable primer-extension product is formed of the detection primer extended to include an extension portion terminated with the labeled chain-terminating nucleotide analogue; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of a detectable label in association with a labeled chain-terminating nucleotide analogue terminating an extension portion of a primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

86. (New) A method for detecting the presence of one or more specific nucleotides at a predetermined target position in a target nucleic acid, the method comprising the steps of:

(a) providing an analyzable amount of the target nucleic acid in a single stranded form;

(b) hybridizing the target nucleic acid with a detection primer to form a target-nucleic-acid/detection-primer hybrid, the detection primer comprising a detection-primer nucleotide sequence having a primer-extension-initiation 3'-end nucleotide which constitutes a 3' end of the detection primer, the detection-primer nucleotide sequence being complementary to a primer-hybridizing nucleotide sequence of the target nucleic acid with a nucleotide in the target nucleic acid complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide, the primer-hybridizing nucleotide sequence of the target nucleic acid extending towards the 3' end of the

target nucleic acid from the primer-end complement nucleotide, the primer-end complement nucleotide being located in the target nucleic acid at a position 3'-ward of the predetermined target position, the position of the primer-end complement nucleotide being subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target nucleic acid in any position between the position of the primer-end complement nucleotide and the predetermined target position;

(c) forming an extension-reaction mixture by exposing the target-nucleic-acid/detection-primer hybrid to an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates of the admixture including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary, the plurality of nucleoside triphosphates of the admixture being such that, if a chain-terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined target position, a detectable nucleotide-identifier primer-extension product is formed of the detection primer extended to include an extension portion terminated with the chain-terminating nucleotide analogue, the detectable nucleotide-identifier primer-extension product being detectably different from the detection primer and from any alternative primer-extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position; and

(d) analyzing the extension-reaction mixture from step (c) for the presence or absence of the detectable nucleotide-identifier primer-extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

87. (New) A method according to claim 86

wherein at least one chain-terminating nucleotide analogue of the admixture of nucleoside

triphosphates of step (c) defines a labeled chain-terminating nucleotide analogue comprising a detectable label or an attachment moiety capable of binding a detectable label, the plurality of nucleoside triphosphates of the admixture being such that, if a labeled chain-terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined target position, the detectable nucleotide-identifier primer-extension product is formed of the detection primer extended to include an extension portion terminated with the labeled chain-terminating nucleotide analogue, the termination of the extension portion of the detectable nucleotide-identifier primer-extension product with the labeled chain-terminating nucleotide analogue rendering the primer-extension product detectably different from the detection primer and from any alternative primer-extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position, and

wherein the step (d) of analyzing the extension-reaction mixture from step (c) for the presence or absence of the detectable nucleotide-identifier primer-extension product includes analyzing the extension-reaction mixture for the presence or absence of a detectable label in association with a labeled chain-terminating nucleotide analogue terminating an extension portion of a primer extension product to determine the respective presence or absence of the detectable nucleotide-identifier primer-extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid.

88. (New) A method according to any of claims 82, 83, 85, or 86, wherein the target nucleic acid is obtained or derived from the cells of a patient and the detection of the specific nucleotide indicates predisposition to a genetic disease in the patient.

89. (New) A method according to any of claims 82, 83, 85, or 86, wherein the analyzable amount of target nucleic acid is obtained by performing an amplification reaction on a sample of nucleic acid.

90. (New) A method according to any of claims 82, 83, 85, or 86 wherein the target

nucleic acid comprises an attachment moiety.

91. (New) A method according to claim 90 wherein the target nucleic acid is immobilized on a solid matrix during step (b).

92. (New) A method according to claim 90 wherein the target nucleic acid is immobilized on a solid matrix during step (c).

93. (New) A method according to any of claims 82, 83, 85, or 86 in which the primer-end complement nucleotide is located in the target nucleic acid at a position immediately adjacent to the predetermined target position.

94. (New) A method according to any of claims 82, 83, 85, or 86 wherein the detection-primer nucleotide sequence is from 10 to 40 nucleotides in length.

95. (New) A method according to either of claims 82 or 84 wherein the nucleoside triphosphates of paragraph (c) include at least two deoxynucleotides, at least one of which deoxynucleotide comprises a detectable label or an attachment moiety capable of binding a detectable label.

96. (New) A method according to any of claims 82, 83, 85, or 86 wherein each deoxynucleotide of the nucleoside triphosphates of paragraph (c) is a deoxyribonucleoside triphosphate selected from the group consisting of dATP, dGTP, dCTP, dUTP, and dTTP.

97. (New) A method according to either of claims 82 or 84 wherein each deoxynucleotide of the nucleoside triphosphates of paragraph (c) is a deoxyribonucleoside triphosphate selected from the group consisting of dATP, dGTP, dCTP, dUTP, and dTTP and in which the detectable label is a radioisotope.

98. (New) A method according to any of claims 82, 83, 85, or 86 wherein each chain-

terminating nucleotide analogue of the nucleoside triphosphates of paragraph (c) is a deoxyribonucleotide selected from the group consisting of ddATP, ddGTP, ddCTP, and ddTTP.

99. (New) A method according to either of claims 85 or 87 wherein each chain-terminating nucleotide analogue of the nucleoside triphosphates of paragraph (c) is a dideoxyribonucleotide selected from the group consisting of ddATP, ddGTP, ddCTP, and ddTTP and in which the detectable label is a fluorescent group.

100. (New) A method according to any of claims 82, 83, 85, or 86, wherein the polymerization agent is a DNA polymerase.

101. (New) A method according to any of claims 82, 83, 85, or 86, wherein the primer extension product is removed from the target nucleic acid prior to analysis.